

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTALAB1643

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\*\*\*\*\* Welcome to STN International \*\*\*\*\*

NEWS 1 Web Page for STN Seminar Schedule - N. America  
NEWS 2 NOV 21 CAS patent coverage to include exemplified prophetic  
substances identified in English-, French-, German-,  
and Japanese-language basic patents from 2004-present  
NEWS 3 NOV 26 MARPAT enhanced with FSORT command  
NEWS 4 NOV 26 CHEMSAFE now available on STN Easy  
NEWS 5 NOV 26 Two new SET commands increase convenience of STN  
searching  
NEWS 6 DEC 01 ChemPort single article sales feature unavailable  
NEWS 7 DEC 12 GBFULL now offers single source for full-text  
coverage of complete UK patent families  
NEWS 8 DEC 17 Fifty-one pharmaceutical ingredients added to PS  
NEWS 9 JAN 06 The retention policy for unread STNmail messages  
will change in 2009 for STN-Columbus and STN-Tokyo  
NEWS 10 JAN 07 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent  
Classification Data  
NEWS 11 FEB 02 Simultaneous left and right truncation (SLART) added  
for CERAB, COMPUAB, ELCOM, and SOLIDSTATE  
NEWS 12 FEB 02 GENBANK enhanced with SET PLURALS and SET SPELLING  
NEWS 13 FEB 06 Patent sequence location (PSL) data added to USGENE  
NEWS 14 FEB 10 COMPENDEX reloaded and enhanced  
NEWS 15 FEB 11 WTEXTILES reloaded and enhanced  
NEWS 16 FEB 19 New patent-examiner citations in 300,000 CA/CAplus  
patent records provide insights into related prior  
art  
NEWS 17 FEB 19 Increase the precision of your patent queries -- use  
terms from the IPC Thesaurus, Version 2009.01  
NEWS 18 FEB 23 Several formats for image display and print options  
discontinued in USPATFULL and USPAT2  
NEWS 19 FEB 23 MEDLINE now offers more precise author group fields  
and 2009 MeSH terms

NEWS 20 FEB 23 TOXCENTER updates mirror those of MEDLINE - more  
precise author group fields and 2009 MeSH terms  
NEWS 21 FEB 23 Three million new patent records blast AEROSPACE into  
STN patent clusters  
NEWS 22 FEB 25 USGENE enhanced with patent family and legal status  
display data from INPADOCDB  
NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that  
specific topic.

All use of STN is subject to the provisions of the STN Customer  
agreement. Please note that this agreement limits use to scientific  
research. Use for software development or design or implementation  
of commercial gateways or other similar uses is prohibited and may  
result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 21:36:02 ON 26 FEB 2009

=> file caplus

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		0.22	0.22

FILE 'CAPLUS' ENTERED AT 21:36:25 ON 26 FEB 2009  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is  
held by the publishers listed in the PUBLISHER (PB) field (available  
for records published or updated in Chemical Abstracts after December  
26, 1996), unless otherwise indicated in the original publications.  
The CA Lexicon is the copyrighted intellectual property of the  
American Chemical Society and is provided to assist you in searching  
databases on STN. Any dissemination, distribution, copying, or storing  
of this information, without the prior written consent of CAS, is  
strictly prohibited.

FILE COVERS 1907 - 26 Feb 2009 VOL 150 ISS 9  
FILE LAST UPDATED: 25 Feb 2009 (20090225/ED)

Caplus now includes complete International Patent Classification (IPC)  
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> s (diphtheria toxin receptor) and (process or processing)

9713 DIPHTHERIA

1 DIPHTHERIAS

9714 DIPHTHERIA

(DIPHTHERIA OR DIPHTHERIAS)

89043 TOXIN

94085 TOXINS

137381 TOXIN

(TOXIN OR TOXINS)

793121 RECEPTOR

730830 RECEPTORS

949788 RECEPTOR

(RECEPTOR OR RECEPTORS)

179 DIPHTHERIA TOXIN RECEPTOR

(DIPHTHERIA(W)TOXIN(W)RECEPTOR)

2760848 PROCESS

1897189 PROCESSES

4122776 PROCESS

(PROCESS OR PROCESSES)

636337 PROCESSING

621 PROCESSINGS

636629 PROCESSING

(PROCESSING OR PROCESSINGS)

L1 29 (DIPHTHERIA TOXIN RECEPTOR) AND (PROCESS OR PROCESSING)

=> s L1 and antibody

343609 ANTIBODY

414371 ANTIBODIES

547407 ANTIBODY

(ANTIBODY OR ANTIBODIES)

L2 8 L1 AND ANTIBODY

=> duplicate remove L2

PROCESSING COMPLETED FOR L2

L3 8 DUPLICATE REMOVE L2 (0 DUPLICATES REMOVED)

=> d L3 bib abs 1-8

L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2008:846759 CAPLUS

DN 149:102676

TI Clearance of influenza virus from the lung depends on migratory langerin  
+CD11b- but not plasmacytoid dendritic cells

AU GeurtsvanKessel, Corine H.; Willart, Monique A. M.; van Rijt, Leonie S.;  
Muskens, Femke; Kool, Mirjam; Baas, Chantal; Thielemans, Kris; Bennett,  
Clare; Clausen, Bjoern E.; Hoogsteden, Henk C.; Osterhaus, Albert D. M.  
E.; Rimmelzwaan, Guus F.; Lambrecht, Bart N.

CS Department of Pulmonary Medicine, Erasmus University Medical Centre  
Rotterdam, Rotterdam, 3015 GE, Neth.

SO Journal of Experimental Medicine (2008), 205(7), 1621-1634

CODEN: JEMEAV; ISSN: 0022-1007

PB Rockefeller University Press

DT Journal

LA English

AB Although dendritic cells (DCs) play an important role in mediating  
protection against influenza virus, the precise role of lung DC subsets,  
such as CD11b- and CD11b+ conventional DCs or plasmacytoid DCs (pDCs), in  
different lung compartments is currently unknown. Early after intranasal  
infection, tracheal CD11b-CD11chi DCs migrated to the mediastinal lymph  
nodes (MLNs), acquiring co-stimulatory mol. in the process.  
This emigration from the lung was followed by an accumulation of  
CD11b+CD11chi DCs in the trachea and lung interstitium. In the MLNs, the  
CD11b+ DCs contained abundant viral nucleoprotein (NP), but these cells  
failed to present antigen to CD4 or CD8 T cells, whereas resident  
CD11b-CD8.alpha.+ DCs presented to CD8 cells, and migratory  
CD11b-CD8.alpha.- DCs presented to CD4 and CD8 T cells. When lung CD11chi  
DCs and macrophages or langerin+CD11b-CD11chi DCs were depleted using  
either CD11c-diphtheria toxin receptor (DTR)  
or langerin-DTR mice, the development of virus-specific CD8+ T cells was  
severely delayed, which correlated with increased clin. severity and a  
delayed viral clearance. 120G8+ CD11cint pDCs also accumulated in the  
lung and LNs carrying viral NP, but in their absence, there was no effect  
on viral clearance or clin. severity. Rather, in pDC-depleted mice, there  
was a redn. in antiviral antibody prodn. after lung clearance of  
the virus. This suggests that multiple DCs are endowed with different  
tasks in mediating protection against influenza virus.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS  
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:568001 CAPLUS

DN 147:8027

TI Mature DC from skin and skin-draining LN retain the ability to acquire and efficiently present targeted antigen

AU Henri, Sandrine; Siret, Carole; Machy, Patrick; Kissenpfennig, Adrien; Malissen, Bernard; Leserman, Lee

CS Centre d'Immunologie de Marseille-Luminy, Faculte des Sciences de Luminy, Aix-Marseille Universite, Marseille, Fr.

SO European Journal of Immunology (2007), 37(5), 1184-1193  
CODEN: EJIMAF; ISSN: 0014-2980

PB Wiley-VCH Verlag GmbH & Co. KGaA

DT Journal

LA English

AB Skin-draining LN contain several phenotypically distinguishable DC populations, which may be immature or mature. Mature DC are generally considered to have lost the capacity to acquire and present newly encountered Ag. Using antibody-opsonized liposomes as Ag carriers, we show that mature DC purified from skin explants are able to efficiently capture liposomes, process Ag encapsulated within them and activate Ag-specific CD4+ T cells. Explant DC from mice with Langerhans cells (LC) expressing the primate diphtheria toxin receptor that were exposed to diphtheria toxin in vivo presented Ag as well as explant DC from wild-type mice, indicating that LC are not required and dermal DC are probably responsible for this presentation. We further show that all DC subtypes from LN that capture opsonized Ag are capable of cross-presenting it to CD8+ T cells. Induction of addnl. maturation in vivo by LPS or treatment with double-stranded RNA did not alter the Ag presentation capacity of the skin or LN DC subtypes. These results suggest that mature DC present in skin-draining LN may play an important role in the induction of primary and/or secondary immune responses against Ag delivered to the LN that they take up by receptor-mediated endocytosis.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:383647 CAPLUS

DN 144:439970

TI Use of fusion proteins that can be taken up by skin cells to deliver therapeutic macromolecules to the bloodstream without injection

IN Mrsny, Randall J.

PA Trinity Biosystems, Inc., USA

SO PCT Int. Appl., 131 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006044205	A2	20060427	WO 2005-US35803	20051004
WO 2006044205	A3	20060908		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005296064	A1	20060427	AU 2005-296064	20051004
CA 2583202	A1	20060427	CA 2005-2583202	20051004
US 20060153798	A1	20060713	US 2005-244349	20051004
EP 1804832	A2	20070711	EP 2005-816333	20051004
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101072584	A	20071114	CN 2005-80041667	20051004
JP 2008515808	T	20080515	JP 2007-534904	20051004
IN 2007CN01897	A	20070831	IN 2007-CN1897	20070504
PRAI US 2004-615970P	P	20041004		
US 2005-684484P	P	20050524		
US 2005-718907P	P	20050919		
WO 2005-US35803	W	20051004		

AB Methods of using peptides that promote cellular uptake and transfer of proteins to deliver macromols. to the bloodstream through the skin without the need for injection are described. The protein of interest is applied as a fusion protein with a receptor binding domain, a transcytosis domain, and a cleavable linker. Generally, the cleavable linker is cleavable by an enzyme present in higher concn. at or near the basal-lateral membrane of a polarized epithelial cell or in the plasma than elsewhere in the body, for example, at the apical side of the polarized epithelial cell. The low rate of delivery of the processed protein can also lessen the risk of developing an immune response to the therapeutic protein (no data). In other aspects, the invention provides nucleic acids encoding delivery

constructs of the invention, kits comprising delivery constructs of the invention, cells expressing delivery constructs of the invention, and methods of using delivery constructs of the invention. Expts. developing the system using green fluorescent protein using cell cultures and rat trachea is demonstrated.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1994:672962 CAPLUS

DN 121:272962

OREF 121:49627a,49630a

TI Biosynthesis and processing by phorbol ester of the cell surface-associated precursor form of heparin-binding EGF-like growth factor

AU Raab, Gerhard; Higashiyama, Shigeki; Hetelekidis, Stella; Abraham, Judith A.; Damm, Deborah; Ono, Minoru; Klagsbrun, Michael

CS Harvard Med. Sch., Children's Hospital, Boston, MA, 02115, USA

SO Biochemical and Biophysical Research Communications (1994), 204(2), 592-7  
CODEN: BBRC A9; ISSN: 0006-291X

PB Academic

DT Journal

LA English

AB Human MDA MB 231 cells were found to synthesize mostly the cell surface-assocd. precursor form of heparin-binding EGF-like growth factor (HB-BGF), a 27-kDa protein. Evidence for this form of HB-EGF included increased fluorescence intensity when cells analyzed by flow cytometry using anti-HB-EGF antibodies, lack of HB-EGF in conditioned medium, and sensitivity to diphtheria toxin, for which HB-EGF is the receptor. Phorbol ester treatment of cells resulted, within 30 min, in loss of cell surface 27 kDa HB-EGF, lack of interaction with anti-HB-EGF antibodies, accumulation of active 21 kDa HB-EGF in conditioned medium, and the acquisition of diphtheria toxin resistance. It was concluded that cell surface-assocd. HB-EGF is the precursor of a bioactive growth factor, is biol. active as the receptor for diphtheria toxin, and is susceptible to rapid processing.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1990:401810 CAPLUS

DN 113:1810

OREF 113:375a,378a

TI Localization of the diphtheria toxin receptor  
-binding domain to the carboxyl-terminal Mr .apprx.6000 region of the toxin

AU Rolf, John M.; Gaudin, Helen M.; Eidels, Leon

CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9048, USA

SO Journal of Biological Chemistry (1990), 265(13), 7331-7

CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB The C-terminal Mr 5982 peptide of diphtheria toxin was prepd. by specific cleavage of the toxin with hydroxylamine and purified by fast-performance liq. chromatog. The identity of the peptide was established by a combination of SDS PAGE anal., reactivity with specific monoclonal antibodies, and N-terminal sequence anal. The Mr 5982 peptide protected highly toxin-sensitive Vero cells from the lethal action of diphtheria toxin. This protection was due to inhibition of the initial step in the cytotoxic process, the binding of toxin to its receptor. Apparently, the Mr 5982 C-terminal region (amino acid residues 482-535) is, or contains, the receptor-binding domain of diphtheria toxin.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1990:50312 CAPLUS

DN 112:50312

OREF 112:8537a,8540a

TI Monoclonal antibodies against Vero cells that protect against diphtheria toxin

AU Ronnberg, Bengt J.; Lidgerding, Burt C.; Middlebrook, John L.

CS Dep. Toxinol., U. S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701, USA

SO Toxicon (1989), 27(10), 1095-104

CODEN: TOXIA6; ISSN: 0041-0101

DT Journal

LA English

AB Mice were immunized with a cell line (Vero) that possesses a high no. of membrane receptors for diphtheria toxin. Spleen cells from these mice were fused with SP2/0-Ag14 cells and 2 cell lines (1A2 and 2D2) isolated by screening for the ability of their secreted antibodies to inhibit binding of radiolabeled diphtheria toxin to Vero cells. These antibodies protected Vero cells from the inhibition of protein synthesis mediated by diphtheria toxin. The antibodies were purified, iodinated, and their binding characteristics investigated. At 4.degree., the assocn. of 1A2 and 2D2 with Vero cells was saturable (KD .apprxeq. 10-8M) and indicated .apprx.106 binding sites/cell. Diphtheria toxin did not inhibit the binding of either radiolabeled antibody . Monoclonal antibody 1A2 completely inhibited 125I-labeled 2D2 binding and vice versa. Trypsin or phospholipase C treatment of Vero cells had no effect on the ability of the monoclonal antibodies to bind to the cells. Apparently, (1) the 2 monoclonal antibodies recognize the same or closely related epitopes and (2) the antibodies bind a domain distinct from the toxin binding site or



to a subcomponent of the diphtheria toxin receptor that is present at many other cell surface sites. These antibodies offer a powerful tool to study the structure, processing, and mode of action of diphtheria toxin receptors.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1981:563541 CAPLUS

DN 95:163541

OREF 95:27235a,27238a

TI Effect of ammonium chloride on receptor-mediated uptake of diphtheria toxin by Vero cells

AU Dorland, Rebecca B.; Middlebrook, John L.; Leppla, Stephen H.

CS US Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701, USA

SO Experimental Cell Research (1981), 134(2), 319-27

CODEN: ECREAL; ISSN: 0014-4827

DT Journal

LA English

AB The mechanism of NH<sub>4</sub>Cl-mediated protection of Vero cells against diphtheria toxin was studied. In the presence of protective concns. of NH<sub>4</sub>Cl, Vero cells bound, internalized, and degraded radiolabeled diphtheria toxin at the same rate and to the same extent as did the control cells. However, when specific antibody was added to NH<sub>4</sub>Cl-treated cells, a fraction of potentially lethal toxin mols. was maintained in a position accessible to antibody neutralization. Apparently, 2 processing mechanisms exists for diphtheria toxin: a nonproductive bulk degrdn. pathway and a productive NH<sub>4</sub>Cl-sensitive pathway by which active fragment is eventually delivered to the cytoplasm.

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1979:605403 CAPLUS

DN 91:205403

OREF 91:33007a,33010a

TI Receptor-mediated internalization and degradation of diphtheria toxin by monkey kidney cells

AU Dorland, Rebecca B.; Middlebrook, John L.; Leppla, Stephen H.

CS US Army Med. Res. Inst. Infect. Dis., Fort Detrick, MD, 21701, USA

SO Journal of Biological Chemistry (1979), 254(22), 11337-42

CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB The ability of a no. of enzymes and chems. to remove cell surface-bound radiolabeled diphtheria toxin was tested; the combination of pronase [9036-06-0] and inositol hexaphosphate [83-86-3] (PIHP) proved most effective. Using PIHP, the kinetics of toxin-cell assocn. at 37.degree. was resolved into 2 components, surface binding and internalization. The

PIHP assay also allowed estn. of the half-time of toxin internalization (.apprx.25 min). An assay involving pptn. of culture supernatants with trichloroacetic acid was developed and used to measure the rate of degrdn. and excretion of cell-assocd. toxin. Agents which markedly inhibited toxin internalization similarly prevented degrdn., implying an intracellular location for the degradative process. The primary radioactive product excreted by Vero cells was monoiodotyrosine. The extent and rate of toxin degrdn. indicated lysosomal involvement. Finally, agents which blocked internalization or degrdn., or both, (e.g. antibody and concanavalin A [11028-71-0]), protected cells from the cytotoxic action of diphtheria toxin, suggesting that these processes are necessary for expression of the biol. effect.

=> s (pro-HB-EGF) and (process or processing)

95621 PRO

1642 PROS

97229 PRO

(PRO OR PROS)

87688 HB

9935 HBS

90726 HB

(HB OR HBS)

30378 EGF

49 EGFS

30389 EGF

(EGF OR EGFS)

31 PRO-HB-EGF

(PRO(W)HB(W)EGF)

2760848 PROCESS

1897189 PROCESSES

4122776 PROCESS

(PROCESS OR PROCESSES)

636337 PROCESSING

621 PROCESSINGS

636629 PROCESSING

(PROCESSING OR PROCESSINGS)

L4 12 (PRO-HB-EGF) AND (PROCESS OR PROCESSING)

=> s L4 and antibody

343609 ANTIBODY

414371 ANTIBODIES

547407 ANTIBODY

(ANTIBODY OR ANTIBODIES)

L5 2 L4 AND ANTIBODY

=> duplicate remove

ENTER L# LIST OR (END):L5

PROCESSING COMPLETED FOR L5

L6 2 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=> d L6 bib abs 1-2

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:920630 CAPLUS

DN 147:421898

TI G protein .beta..gamma. subunits augment UVB-induced apoptosis by stimulating the release of soluble heparin-binding epidermal growth factor from human keratinocytes

AU Seo, MiRan; Lee, Mi-Jeong; Heo, Jin Hee; Lee, Yun-Il; Kim, Yeni; Kim, So-Young; Lee, Eun-So; Juhn, Yong-Sung

CS Department of Biochemistry and Molecular Biology and Cancer Research Institute, Seoul National University College of Medicine, Seoul, 110-779, S. Korea

SO Journal of Biological Chemistry (2007), 282(34), 24720-24730

CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB UV radiation induces various cellular responses by regulating the activity of many UV-responsive enzymes, including MAPKs. The .beta..gamma. subunit of the heterotrimeric GTP-binding protein (G.beta..gamma.) was found to mediate UV-induced p38 activation via epidermal growth factor receptor (EGFR). However, it is not known how G.beta..gamma. mediates the UVB-induced activation of EGFR, and thus we undertook this study to elucidate the mechanism. Treatment of HaCaT-immortalized human keratinocytes with conditioned medium obtained from UVB-irradiated cells induced the phosphorylations of EGFR, p38, and ERK but not that of JNK. Blockade of heparin-binding EGF-like growth factor (HB-EGF) by neutralizing antibody or CRM197 toxin inhibited the UVB-induced activations of EGFR, p38, and ERK in normal human epidermal keratinocytes and in HaCaT cells. Treatment with HB-EGF also activated EGFR, p38, and ERK. UVB radiation stimulated the processing of pro-HB-EGF and increased the secretion of sol. HB-EGF in medium, which was quantified by immunoblotting and protein staining. In addn., treatment with CRM179 toxin blocked UV-induced apoptosis, but HB-EGF augmented this apoptosis. Moreover, UVB-induced apoptosis was reduced by inhibiting EGFR or p38. The overexpression of G.beta.1.gamma.2 increased EGFR-activating activity and sol. HB-EGF content in conditioned medium, but the sequestration of G.beta..gamma. by the carboxyl terminus of G protein-coupled receptor kinase 2 (GRK2ct) produced the opposite effect. The activation of Src increased UVB-induced,

G.beta..gamma.-mediated HB-EGF secretion, but the inhibition of Src blocked that. Overexpression of G.beta..gamma. increased UVB-induced apoptosis, and the overexpression of GRK2ct decreased this apoptosis. We conclude that G.beta..gamma. mediates UVB-induced human keratinocyte apoptosis by augmenting the ectodomain shedding of HB-EGF, which sequentially activates EGFR and p38.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2001:84701 CAPLUS

DN 134:126503

TI Angiotensin AT1 and AT2 receptors differentially regulate angiopoietin-2 and vascular endothelial growth factor expression and angiogenesis by modulating heparin binding-epidermal growth factor (EGF)-mediated EGF receptor transactivation

AU Fujiyama, Soichiro; Matsubara, Hiroaki; Nozawa, Yoshihisa; Maruyama, Katsuya; Mori, Yasukiyo; Tsutsumi, Yoshiaki; Masaki, Hiroya; Uchiyama, Yoko; Koyama, Yoko; Nose, Atsuko; Iba, Osamu; Tateishi, Eriko; Ogata, Nahoko; Jyo, Nobuo; Higashiyama, Shigeki; Iwasaka, Toshiji

CS Dep. Medicine II and Ophthalmology, Kansai Medical Univ., Ooka, Japan

SO Circulation Research (2001), 88(1), 22-29

CODEN: CIRUAL; ISSN: 0009-7330

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Angiotensin II (Ang II)-mediated signals are transmitted via heparin binding epidermal growth factor (EGF)-like growth factor (HB-EGF) release followed by transactivation of EGF receptor (EGFR). Although Ang II and HB-EGF induce angiogenesis, their link to the angiopoietin (Ang)-Tie2 system remains undefined. We tested the effects of Ang II on Ang1, Ang2, or Tie2 expression in cardiac microvascular endothelial cells expressing the Ang II receptors AT1 and AT2. Ang II significantly induced Ang2 mRNA accumulations without affecting Ang1 or Tie2 expression, which was inhibited by protein kinase C inhibitors and by intracellular Ca<sup>2+</sup> chelating agents. Ang II transactivated EGFR via AT1 and inhibition of EGFR abolished the induction of Ang2. Ang II caused processing of pro-HB-EGF in a metalloproteinase-dependent manner to stimulate maturation and release of HB-EGF. Neutralizing anti-HB-EGF antibody blocked EGFR phosphorylation by Ang II. Ang II also upregulated vascular endothelial growth factor (VEGF) expression in an HB-EGF/EGFR-dependent manner. AT2 inhibited AT1-mediated Ang2 expression and phosphorylation of EGFR. In an in vivo corneal assay, AT1 induced angiogenesis in an HB-EGF-dependent manner and enhanced the angiogenic activity of VEGF. Although neither

Ang2 nor Ang1 alone induced angiogenesis, sol. Tie2-Fc that binds to angiopoietins attenuated AT1-mediated angiogenesis. These findings suggested that (1) Ang II induces Ang2 and VEGF expression without affecting Ang1 or Tie2 and (2) AT, stimulates processing of pro-HB-EGF by metalloproteinases, and the released HB-EGF transactivates EGFR to induce angiogenesis via the combined effect of Ang2 and VEGF, whereas AT2 attenuates them by blocking EGFR phosphorylation. Thus, Ang II is involved in the VEGF-Ang-Tie2 system via HB-EGF-mediated EGFR transactivation, and this link should be considerable in pathol. conditions in which collateral blood flow is required.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s (pro-HB-EGF) and (cleave or cleavage or cleaving)

95621 PRO

1642 PROS

97229 PRO

(PRO OR PROS)

87688 HB

9935 HBS

90726 HB

(HB OR HBS)

30378 EGF

49 EGFS

30389 EGF

(EGF OR EGFS)

31 PRO-HB-EGF

(PRO(W)HB(W)EGF)

12095 CLEAVE

9680 CLEAVES

20829 CLEAVE

(CLEAVE OR CLEAVES)

232484 CLEAVAGE

6114 CLEAVAGES

235383 CLEAVAGE

(CLEAVAGE OR CLEAVAGES)

13202 CLEAVING

2 CLEAVINGS

13203 CLEAVING

(CLEAVING OR CLEAVINGS)

L7 6 (PRO-HB-EGF) AND (CLEAVE OR CLEAVAGE OR CLEAVING)

=> s L7 and antibody

343609 ANTIBODY  
414371 ANTIBODIES  
547407 ANTIBODY  
(ANTIBODY OR ANTIBODIES)

L8 1 L7 AND ANTIBODY

=> d L8 bib abs 1

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2003:389324 CAPLUS

DN 139:115428

TI TACE cleavage of proamphiregulin regulates GPCR-induced  
proliferation and motility of cancer cells

AU Gschwind, Andreas; Hart, Stefan; Fischer, Oliver M.; Ullrich, Axel

CS Department of Molecular Biology, Max-Planck Institute of Biochemistry,  
Martinsried, D-82152, Germany

SO EMBO Journal (2003), 22(10), 2411-2421

CODEN: EMJODG; ISSN: 0261-4189

PB Oxford University Press

DT Journal

LA English

AB Communication between G protein-coupled receptor (GPCR) and epidermal growth factor receptor (EGFR) signaling systems involves cell surface proteolysis of EGF-like precursors. The underlying mechanisms of EGFR signal transactivation pathways, however, are largely unknown. We demonstrate that in squamous cell carcinoma cells, stimulation with the GPCR agonists LPA or carbachol specifically results in metalloprotease cleavage and release of amphiregulin (AR). Moreover, AR gene silencing by siRNA or inhibition of AR biol. activity by neutralizing antibodies and heparin prevents GPCR-induced EGFR tyrosine phosphorylation, downstream mitogenic signaling events, cell proliferation, migration and activation of the survival mediator Akt/PKB. Therefore, despite some functional redundancy among EGF family ligands, the present study reveals a distinct and essential role for AR in GPCR-triggered cellular responses. Furthermore, we present evidence that blockade of the metalloprotease-disintegrin tumor necrosis factor- $\alpha$ -converting enzyme (TACE) by the tissue inhibitor of metalloprotease-3, a dominant-neg. TACE mutant or RNA interference suppresses GPCR-stimulated AR release, EGFR activation and downstream events. Thus, TACE can function as an effector of GPCR-mediated signaling and represents a key element of the cellular receptor cross-talk network.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS  
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S (diphtheria toxin receptor) and (cleave or cleavage or cleaving)

9713 DIPHTHERIA  
1 DIPHTHERIAS  
9714 DIPHTHERIA  
(DIPHTHERIA OR DIPHTHERIAS)  
89043 TOXIN  
94085 TOXINS  
137381 TOXIN  
(TOXIN OR TOXINS)  
793121 RECEPTOR  
730830 RECEPTORS  
949788 RECEPTOR  
(RECEPTOR OR RECEPTORS)  
179 DIPHTHERIA TOXIN RECEPTOR  
(DIPHTHERIA(W)TOXIN(W)RECEPTOR)  
12095 CLEAVE  
9680 CLEAVES  
20829 CLEAVE  
(CLEAVE OR CLEAVES)  
232484 CLEAVAGE  
6114 CLEAVAGES  
235383 CLEAVAGE  
(CLEAVAGE OR CLEAVAGES)  
13202 CLEAVING  
2 CLEAVINGS  
13203 CLEAVING  
(CLEAVING OR CLEAVINGS)

L9 8 (DIPHTHERIA TOXIN RECEPTOR) AND (CLEAVE OR CLEAVAGE OR CLEAVING)

=> s L9 and antibody

343609 ANTIBODY  
414371 ANTIBODIES  
547407 ANTIBODY  
(ANTIBODY OR ANTIBODIES)

L10 3 L9 AND ANTIBODY

=> duplicate remove L10

PROCESSING COMPLETED FOR L10

L11 3 DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)

=> d L11 bib abs 1-3

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:383647 CAPLUS

DN 144:439970

TI Use of fusion proteins that can be taken up by skin cells to deliver  
therapeutic macromolecules to the bloodstream without injection

IN Mrsny, Randall J.

PA Trinity Biosystems, Inc., USA

SO PCT Int. Appl., 131 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006044205	A2	20060427	WO 2005-US35803	20051004
WO 2006044205	A3	20060908		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005296064	A1	20060427	AU 2005-296064	20051004
CA 2583202	A1	20060427	CA 2005-2583202	20051004
US 20060153798	A1	20060713	US 2005-244349	20051004
EP 1804832	A2	20070711	EP 2005-816333	20051004
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101072584	A	20071114	CN 2005-80041667	20051004
JP 2008515808	T	20080515	JP 2007-534904	20051004
IN 2007CN01897	A	20070831	IN 2007-CN1897	20070504
PRAI US 2004-615970P	P	20041004		
US 2005-684484P	P	20050524		
US 2005-718907P	P	20050919		
WO 2005-US35803	W	20051004		

AB Methods of using peptides that promote cellular uptake and transfer of  
proteins to deliver macromols. to the bloodstream through the skin without  
the need for injection are described. The protein of interest is applied  
as a fusion protein with a receptor binding domain, a transcytosis domain,  
and a cleavable linker. Generally, the cleavable linker is cleavable by  
an enzyme present in higher concn. at or near the basal-lateral membrane  
of a polarized epithelial cell or in the plasma than elsewhere in the



body, for example, at the apical side of the polarized epithelial cell. The low rate of delivery of the processed protein can also lessen the risk of developing an immune response to the therapeutic protein (no data). In other aspects, the invention provides nucleic acids encoding delivery constructs of the invention, kits comprising delivery constructs of the invention, cells expressing delivery constructs of the invention, and methods of using delivery constructs of the invention. Expts. developing the system using green fluorescent protein using cell cultures and rat trachea is demonstrated.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2002:937303 CAPLUS

DN 138:20443

TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

IN Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin

PA Takara Bio Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 386 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002355079	A	20021210	JP 2002-69354	20020313
PRAI JP 2001-73183	A	20010314		
JP 2001-74993	A	20010315		
JP 2001-102519	A	20010330		

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prepg. a nucleic acid sample contg. mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-.beta. estradiol (E2), were found in mice by DNA chip anal.

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1990:401810 CAPLUS

DN 113:1810

OREF 113:375a,378a

TI Localization of the diphtheria toxin receptor

-binding domain to the carboxyl-terminal Mr .apprx.6000 region of the toxin

AU Rolf, John M.; Gaudin, Helen M.; Eidels, Leon

CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9048, USA

SO Journal of Biological Chemistry (1990), 265(13), 7331-7

CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB The C-terminal Mr 5982 peptide of diphtheria toxin was prepd. by specific cleavage of the toxin with hydroxylamine and purified by fast-performance liq. chromatog. The identity of the peptide was established by a combination of SDS PAGE anal., reactivity with specific monoclonal antibodies, and N-terminal sequence anal. The Mr 5982 peptide protected highly toxin-sensitive Vero cells from the lethal action of diphtheria toxin. This protection was due to inhibition of the initial step in the cytotoxic process, the binding of toxin to its receptor. Apparently, the Mr 5982 C-terminal region (amino acid residues 482-535) is, or contains, the receptor-binding domain of diphtheria toxin.